

***What is claimed is:***

1. A method of identifying one or more markers for lung disease, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having lung disease, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for lung disease; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals not having lung disease,

wherein those compared transcripts which display differing levels in the comparison of step b) are identified as being markers for lung disease.

2. A method of identifying one or more markers for lung disease, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having lung disease, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for lung disease; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals having lung disease,

wherein those compared transcripts which display the same levels in the comparison of step b) are identified as being markers for lung disease.

3. A method of identifying one or more markers of a stage of lung disease progression or regression, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having a stage of lung disease, wherein said one or more individuals are at the same progressive or regressive stage of lung disease, and wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for determining the stage of progression or regression of lung disease, and;

b) comparing the level of each of said one or more gene transcripts from said step a)

with the level of each of said one or more genes transcripts in blood obtained from one or more individuals who are at a progressive or regressive stage of lung disease distinct from that of said one or more individuals of step a),

wherein those compared transcripts which display differing levels in the comparison of  
5 step b) are identified as being markers for the stage of progression or regression of lung disease.

4. A method of identifying one or more markers of a stage of lung disease progression or regression, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

10 a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having a stage of lung disease, wherein said one or more individuals are at the same progressive or regressive stage of lung disease, and wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for determining the stage of progression or regression of lung disease, and;

15 b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals who are at a progressive or regressive stage of lung disease identical to that of said one or more individuals of step a),

wherein those compared transcripts which display the same levels in the comparison of  
20 step b) are identified as being markers for the stage of progression or regression of lung disease.

5. The method of any one of claims 1 - 4, wherein each of said one or more markers identifies one or more transcripts of one or more non immune response genes.

6. The method of any one of claims 1 - 4, wherein each of said one or more markers  
25 identifies a transcript of a gene expressed by non-blood tissue.

7. The method of any one of claims 1 - 4, wherein each of said one or more markers identifies a transcript of a gene expressed by non-lymphoid tissue.

8. The method of any one of claims 1-4, wherein said one or more markers identifies one or more genes selected from the group of genes listed in Table 3I.

9. A method of diagnosing or prognosing lung disease in an individual, comprising the steps of:

5 a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from  
10 one or more individuals not having lung disease,

wherein detecting a difference in the levels of each of said one or more gene transcripts in the comparison of step b) is indicative of lung disease in the individual of step a).

10. A method of diagnosing or prognosing lung disease in an individual, comprising the  
15 steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood  
20 according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having lung disease,

wherein detecting the same levels of each of said one or more gene transcripts in the comparison of step b) is indicative of lung disease in the individual of step a).

11. A method of determining a stage of disease progression or regression in an individual  
25 having lung disease, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual having lung disease, wherein said one or more gene transcripts correspond to said one or more markers of claim 3 and claim 4, and

b) comparing the level of each if said one or more gene transcripts in said blood

according to step a) with the level of each of said one or more gene transcripts in blood obtained from one or more individuals who each have been diagnosed as being at the same progressive or regressive stage of lung disease,

wherein the comparison from step b) allows the determination of the stage of lung disease progression or regression in an individual.

12. A method of diagnosing or prognosing lung disease in an individual, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts corresponds to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having lung disease,

c) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals not having lung disease

d) determining whether the level of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with levels of said transcripts in step c),

wherein said determination is indicative of said individual of step a) having lung disease.

13. A method of determining a stage of disease progression or regression of lung disease in an individual, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts corresponds to said one or more markers of claim 3 and claim 4, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having said stage of lung disease,

c) comparing the level of each of said one or more gene transcripts in said blood

according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals not having said stage of lung disease,

d) determining whether the level of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with levels of said transcripts in step c),

wherein said determination is indicative of said individual of step a) having said stage of lung disease.

14. The method of any one of claims 9 - 13, wherein each of said one or more markers identifies a transcript of a gene selected from the group consisting of the genes listed in Table

3I.

15. The method of any one of claims 1 - 4 and 9 - 13, wherein said one or more gene transcripts are transcribed from one or more genes selected from the group consisting of:

a) non-immune response genes,

b) genes expressed by non blood tissue, and

c) genes expressed by non lymphoid tissue.

16. The method of any one of claims 1 - 4 and 9 - 13, wherein said blood comprises a blood sample obtained from said one or more individuals.

17. The method of claim 16, wherein said blood sample consists of whole blood.

18. The method of claim 16, wherein said blood sample consists of a drop of blood.

19. The method of claim 16, wherein said blood sample consists of blood that has been lysed.

20. The method of claim 16, further comprising the step of isolating RNA from said blood samples.

21. The method of any one of claims 1 - 4 and 9 - 13, wherein the step of determining the level of each of said one or more gene transcripts comprises quantitative RT-PCR (QRT-PCR), wherein said one or more transcripts are from step a) and/or step b) of claims 1 - 4 and 9 - 13.

22. The method of claim 21, wherein said QRT-PCR comprises primers which hybridize to said one or more transcripts or the complement thereof, wherein said one or more transcripts are from step a) and/or step b) of claims 1 - 4 and 9 - 13.

23. The method of claim 22, wherein said primers are 15-25 nucleotides in length.

5 24. The method of claim 22, wherein said primers hybridize to one or more transcripts of one or more genes selected from the group of genes listed in Table 3I, or the complement thereof.

25. The method of any one of claims 1 - 4 and 9 - 13, wherein the step of determining the level of each of said one or more gene transcripts comprises hybridizing a first plurality of  
10 isolated nucleic acid molecules that correspond to said one or more transcripts, to an array comprising a second plurality of isolated nucleic acid molecules.

26. The method of claim 25, wherein said first plurality of isolated nucleic acid molecules comprises RNA, DNA, cDNA, PCR products or ESTs.

27. The method of claim 25, wherein said array comprises a plurality of isolated nucleic  
15 acid molecules comprising RNA, DNA, cDNA, PCR products or ESTs.

28. The method of claim 27, wherein said array comprises two or more of the markers of claim 1.

29. The method of claim 27, wherein said array comprises two or more of the markers of claim 2.

20 30. The method of claim 27, wherein said array comprises two or more of the markers of claim 3.

31. The method of claim 27, wherein said array comprises two or more of the markers of claim 4.

32. The method of claim 27, wherein said array comprises a plurality of nucleic acid  
25 molecules that correspond to genes of the human genome.

33. The method of claim 27, wherein said array comprises a plurality of nucleic acid molecules that correspond to two or more genes selected from the group of genes listed in Table 3I.

34. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 1.

35. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 2.

36. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 3.

37. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 4.

38. The method of claim 26, wherein said ESTs comprise a length greater than 100 nucleotides.

39. An array consisting essentially of the plurality of nucleic acid molecules of claim 34.

40. An array consisting essentially of the plurality of nucleic acid molecules of claim 35.

41. An array consisting essentially of the plurality of nucleic acid molecules of claim 36.

42. An array consisting essentially of the plurality of nucleic acid molecules of claim 37.

43. A kit for diagnosing or prognosing lung disease comprising:

a) two gene-specific priming means designed to produce double stranded DNA

complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

5 44. A kit for monitoring a course of therapeutic treatment of lung disease, comprising:

a) two gene-specific priming means designed to produce double stranded DNA

complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3 and claim 4; wherein said first priming means

contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said

10 gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means;

15 wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

45. A kit for monitoring progression or regression of lung disease, comprising:

a) two gene-specific priming means designed to produce double stranded DNA

complementary to a gene that corresponds to a marker selected from the group consisting of

20 the markers of claim 1, claim 2, claim 3 and claim 4; wherein said first priming means

contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said

gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

25 c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.



46. The kit of any one of claims 43 - 45 wherein said gene-specific priming means are complementary to a gene selected from the group of genes listed in Table 3I;

47. A plurality of nucleic acid molecules that identify or correspond to two or more genes selected from the group of genes listed in Table 3I.

5 48. The method of claim 27, wherein said ESTs comprise a length comprise a length of greater than 100 nucleotides.